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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/832,069

Applicant(s)

RUNGE ET AL.

Examiner

Jeanine A Goldberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed June 4, 2003. Currently, claims 6-10 are pending.
2. The examiner called Benjamin Adler on June 26, 2003 to indicate that upon reconsideration the examiner felt that the claims were not allowable as set forth below.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

It is noted that no IDS has been filed and applicants did not respond to the notice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 6-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Yan et al. (Circulation, Vol. 96, No. 8, Suppl. P. I605, October 21, 1997)

The instant specification defines "oxidative stress" to refer to pathophysiological effects of reactive oxygen species, such as H₂O₂, superoxide, peroxynitrate, and other reactive oxygen species (page 25 of the specification).

Yan et al. (herein referred to as Yan) teaches in vivo evidence of the relationship of reactive oxygen species and mitochondrial DNA damage in atherosclerosis. Specifically, Yan teaches assaying both diseased and normal human aortic tissues for DNA damage using a gene-specific quantitative PCR assay. Yan teaches designing primers to amplify a fragment of the human mitochondrial genome and a nuclear fragment within the beta-globin gene. Fresh surgical specimens of normal and atherosclerotic human aorta were immediately frozen in liquid nitrogen. Yan reports that mtDNA damage detected in atherosclerotic tissue was 2 to 5 fold higher than that of human aortic samples without evidence of atherosclerosis. The evidence suggest that the average DNA lesion frequency in the mitochondrial genome was approximately four times higher than that in the nuclear B-globin gene (limitations of Claim 6, 7, 8, 10). Yan teaches that the levels of H₂O₂ and O₂⁻ were assessed using a peroxidase-H₂O₂ formation assay. The results of Yan suggest that an increase in H₂O₂ and O₂⁻ levels in patients with CAD compared to those without CAD, consistent with a correlation between mtDNA damage and ROS generation. Yan teaches that the data suggest that oxidative mtDNA damage may play a role in atherosclerotic lesion development.

Therefore, since Yan teaches an association between an increase in H₂O₂ and O₂⁻ levels in patients with CAD compared to those without CAD which is consistent with a correlation between mtDNA damage and ROS generation, Yan inherently teaches a

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method of assaying for oxidative stress, as defined by the instant specification and the art, by detecting mtDNA damage.

Conclusion

5. **Claims 6-10 are rejected.**

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.


A) Corral-Debrinski et al (Mutation Research, Vol. 275, pages 169-180, 1992).

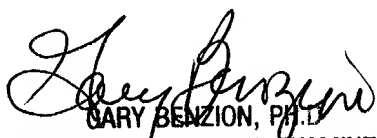
Corral-Debrinski et al. (herein referred to as Corral-Debrinski) teaches an association of mitochondrial DNA damage with coronary atherosclerotic heart disease. Corral- Debrinski teaches the H₂O₂ can react with superoxide to generate hydroxyl radical (OH⁻) which are extremely reactive (page 170, col. 2). The close proximity of the mtDNA to these reactive molecules in the inner mitochondrial membrane and the deficiency in mtDNA repair systems result in preferential oxidative damage to the mtDNA (page 170, col. 2).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Jeanine Goldberg
June 26, 2003


GARY BENZION, Ph.D.
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